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PATENT APPLICATION

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Director-General, Japanese Patent Office

1. Title of the Invention

A method for the production of tetrahydro-isoquinoline derivatives

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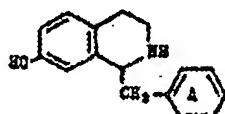
Specification

Title of the Invention

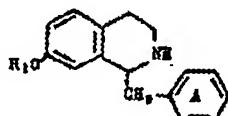
A method for the production of tetrahydroisoquinoline derivatives

Scope of Claim

A method for the production of tetrahydroisoquinoline derivatives represented by the general formula



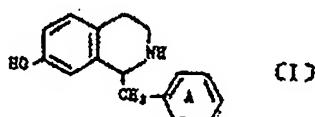
(where, ring A represents a phenyl group substituted with three lower alkoxy groups), which is characterized in that the 7-acyloxy-1-benzyl-1,2,3,4-tetrahydroisoquinoline derivatives represented by the general formula



(where R₁ represents an organic acyl group and A has the same meaning as above) are subjected to hydrolysis.

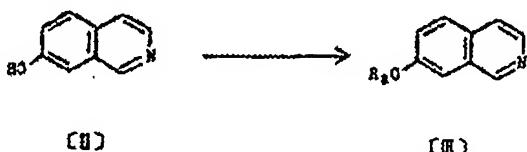
Detailed Description of the Invention

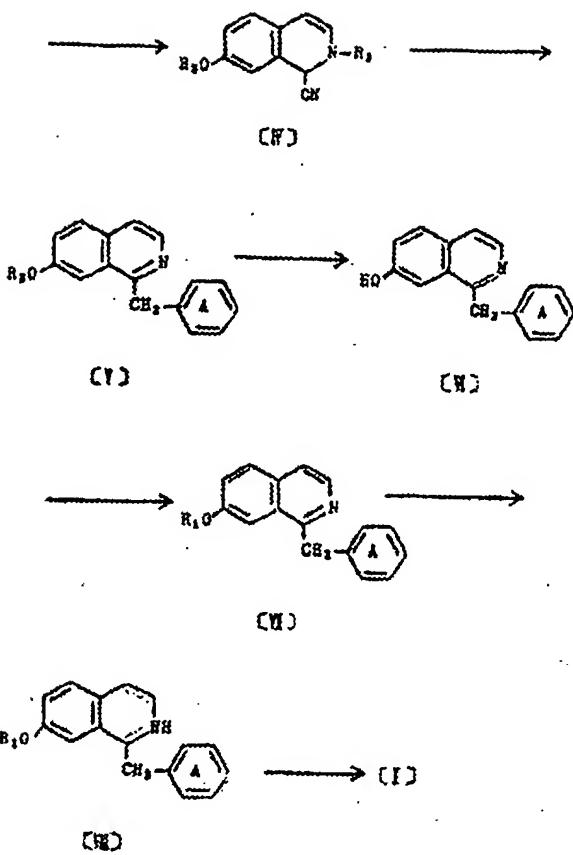
The present invention relates to a method for the production of the novel tetrahydroisoquinoline derivatives represented by general formula



(where, ring A represents a phenyl group substituted with three lower alkoxy groups).

It is already known from, for example, West German Laid-Open Patent Publication No. 2162563 and Japanese Patent Publication No. 48-7114 that 6-hydroxy-1-trimethoxybenzyl-1,2,3,4-tetrahydroisoquinoline and the like are useful compounds which have a vasodilating action. However, while the production of these compounds having a hydroxy group at the 6-position on the 1,2,3,4-tetrahydroisoquinoline skeletal structure is comparatively easy, the production of compounds with a hydroxy group only at the 7-position is not easy. As a result of research, the present inventors have succeeded in producing various compounds with the hydroxy group only at the 7-position and, furthermore, they have discovered that amongst these compounds the 1,2,3,4-tetrahydroisoquinoline derivatives [I] which have a trialkoxybenzyl group at the 1-position have a markedly more powerful blood flow increasing action than the aforesaid known compounds. For example, when compared to the corresponding 6-hydroxy compound, 7-hydroxy-1-(3,4,5-trimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (hydrochloride) has at least a 10 times more powerful blood flow increasing action in the common carotid artery of the dog. In accordance with the present invention, the compounds [I] can be produced by the method represented by the following reaction scheme.





(Here, R_1 and R_3 represent the same or different organic acyl groups and R_2 is an aralkyl group. Ring A has the same meaning as above.)